



THE UNIVERSITY *of* EDINBURGH

Edinburgh Research Explorer

Disappearing hemipelvis Low grade osteosarcoma, an unusual and poorly described variant of Paget's Sarcoma

Citation for published version:

Stevens, JM, Flower, H, Salter, D & Patton, JT 2018, 'Disappearing hemipelvis Low grade osteosarcoma, an unusual and poorly described variant of Paget's Sarcoma', *Journal of Pediatric Orthopaedics*, vol. 15, no. 2, pp. 571-577. <https://doi.org/10.1016/j.jor.2018.05.017>

Digital Object Identifier (DOI):

[10.1016/j.jor.2018.05.017](https://doi.org/10.1016/j.jor.2018.05.017)

Link:

[Link to publication record in Edinburgh Research Explorer](#)

Document Version:

Peer reviewed version

Published In:

Journal of Pediatric Orthopaedics

General rights

Copyright for the publications made accessible via the Edinburgh Research Explorer is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy

The University of Edinburgh has made every reasonable effort to ensure that Edinburgh Research Explorer content complies with UK legislation. If you believe that the public display of this file breaches copyright please contact openaccess@ed.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.



Disappearing hemipelvis: Low grade osteosarcoma, an unusual and poorly described variant of Paget's Sarcoma

AUTHORS:

Jarrad Stevens¹, Hannah Flower², Donald Salter³, James T Patton¹

Jarrad Stevens, MBBS, FRACS, FAOrthA

Hannah Flower, BMedSci

Donald Salter, MD, FRCPath, FRCPEd

James T Patton, FRCS, FRCSEd (Tr & Orth)

INSTITUTION:

¹ Department of Surgery, Orthopaedics, Royal Infirmary Edinburgh

² School of Medicine, University of Edinburgh

³ Department of Pathology, Royal Infirmary Edinburgh

CORRESPONDENCE:

drjarradstevens@hotmail.com

DISCLAIMER:None

Conflict of Interest: No conflicts

Introduction:

Paget's sarcomatous transformation is a rare and potentially fatal complication of Paget's disease. It accounts for approximately 5% of all osteosarcomas [1]. Histologically, it has been described as a high-grade and extremely aggressive malignancy. We present the unusual radiographs of a patient diagnosed with a low-grade Paget's osteosarcoma, a very rare and poorly described variant of the disease.

In this radiographic review, we illustrate the unusual features of localised low-grade Paget's osteosarcoma of the pelvis and proximal femur, with lytic resorption and complete loss of the hemi-pelvis. We also identify the histological features that are consistent with low-grade Paget's Osteosarcoma.

Case Presentation:

A previously healthy 73-year-old man presented to the orthopaedic department for management of an ankle fracture. During an admission to hospital for this, he raised concern regarding ongoing left hip pain. Our patient detailed a prolonged history of gait disturbance and discomfort on weight-bearing, but described no pain at rest or at night. Subsequent radiographs demonstrated a lytic lesion on the left side of his pelvis, involving the ischium (Figure 1). A bone scan showed evidence of markedly increased uptake at this site.

With the exception of gastroesophageal reflux disease and hypertension, no significant past medical history was noted. The patient did not report a family history of Paget's disease, however as he was adopted an accurate assessment was difficult to obtain.

Given the concerning areas of lysis and activity on bone scan, open biopsy was organised. The histological appearance was suggestive of active Paget's disease (Histology slide 1), but with no obvious evidence of malignancy. In spite of this, additional biopsies were organised, owing to a strong clinical suspicion of underlying malignancy.

A second core biopsy included new woven bone and showed irregular trabeculae of pre-existing lamellar bone undergoing aggressive osteoclastic resorption. The intervening marrow was almost completely replaced by fibro-connective tissue and areas of haemopoiesis. Again there were no obvious features of malignancy.

The patient was placed under radiographic surveillance. The radiographs taken over the five years since his initial presentation (Figures 2-6) record the unusual progression of the disease. Subcapital fracture was followed by subtrochanteric femoral fracture and complete resorption of the hemipelvis and proximal femur. A third biopsy, taken three years after the initial presentation, was unlike the previous two biopsies. The morphological features were consistent with low to intermediate grade spindle cell sarcoma, with no convincing lineage of differentiation (Histology slide 2). Subsequently, the case was presented to the pathologists at the multidisciplinary sarcoma meeting and discussion was held at the Scottish National Sarcoma meeting. A diagnosis of an exceptionally rare low-grade Paget's osteosarcoma was made. This is an unusual and poorly described variant of Paget's osteosarcoma, which normally presents as high-grade and extremely aggressive. Review by the Professor of pathology at the Manchester Royal Infirmary provided consensus on the diagnosis.

Zoledronic Acid was first prescribed following diagnosis of Paget's disease. This had an good initial result with our patient improving in both pain and ambulation. Further

progression of the disease process lead to two further treatments with Zoledronic Acid. After still further progression the patient was commenced on three monthly injections of Denosumab however this also proved ineffective and injections were stopped. Following diagnosis of osteosarcoma, treatment options including resection, chemotherapy and radiotherapy were discussed, however the patient and the team decided non-operative symptomatic treatment was the best option.

Discussion:

In 1877, Sir James Paget first described a case of *Osteitis Deformans*: an inflammation of the bone [2]. His name would become eponymous with the condition. Today the prevalence of Paget's disease is approximately 4-5%; Barker et al report a 5.4% prevalence in British adults older than 55 years [3-5].

Paget's disease is characterised by local disruption of normal bone remodelling. Sarcomatous transformation is a rare event in Paget's disease [6]. The reported incidence ranges from 0.15% to 1% [7,8]. The conventional high-grade presentation of Paget's osteosarcoma is extensive, both locally and systemically [9]. As such, the prognosis of high-grade Paget osteosarcoma is poor; few patients survive beyond 5 years [1,6,10,11].

Low-grade, also known as intraosseous well-differentiated osteosarcoma, is an intramedullary bone-producing tumour that accounts for approximately 1-2% of all osteosarcomas [14]. Low-grade osteosarcomas have been reported to have a better prognosis than high-grade variants, with slower growth and increased survival after treatment [12]. However, the low incidence of low-grade osteosarcomas and the

overlap in presentation with benign conditions often leads to a delay in diagnosis and treatment [13].

Given the rarity of this presentation, it may be reasonable to question whether low-grade osteosarcoma is a form of Paget's sarcomatous transformation, or whether it is a separate disease process. A further example in the literature is that of Franchi et al [12]. Two patients presented with characteristics of Paget's disease and subsequently developed low-grade osteosarcoma. As Paget's osteosarcomas are assumed to be high-grade, the authors concluded that although the low-grade osteosarcomas had histological features suggestive of Paget's disease, it could not be Paget's sarcomatous transformation [12]. No other cases of low-grade Paget's osteosarcoma in the literature could be found.

Conclusion:

This is a very rare presentation of a poorly described variant of Paget's osteosarcoma. Whilst it is typically high grade and extremely aggressive, this low-grade tumour has been exceptionally aggressive in its resorption of bone, leading to complete loss of the hemipelvis and proximal femur. We present this unique radiographic series for review by surgeons with an interest in this disorder.

Figure 1: Radiograph AP Pelvis at presentation

Figure 2: Radiograph AP Pelvis at 1 year post presentation

Figure 3: Radiograph AP Pelvis at 2 years post presentation

Figure 4: Radiograph AP Pelvis at 3 years post presentation

Figure 5: Radiograph AP Pelvis at 4 years post presentation

Figure 6: Radiograph AP Pelvis at 5 years post presentation

Histology Slide 1: Histology shows bone within which there is florid osteoclastic resorption coupled with marked osteoblastic activity. There is mild peritrabecular fibrosis. The appearances are consistent with Paget's Disease of bone. H/E stain, original magnification x20.

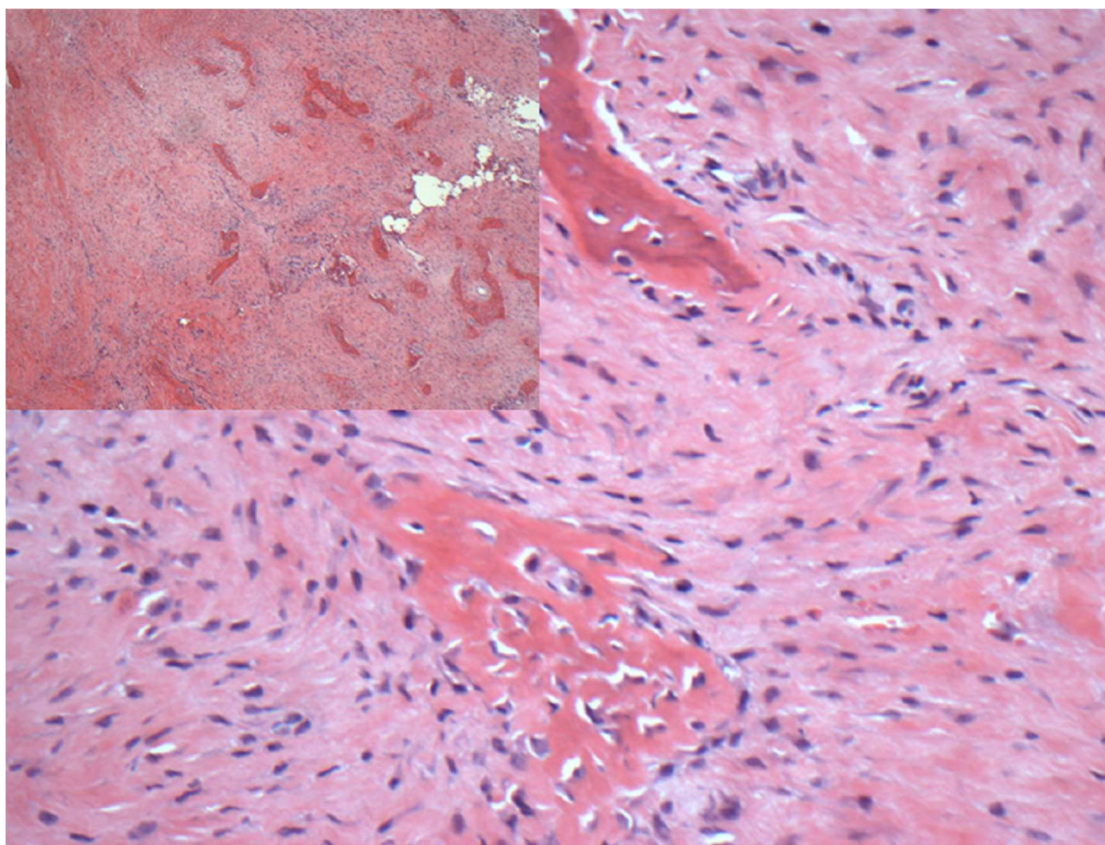
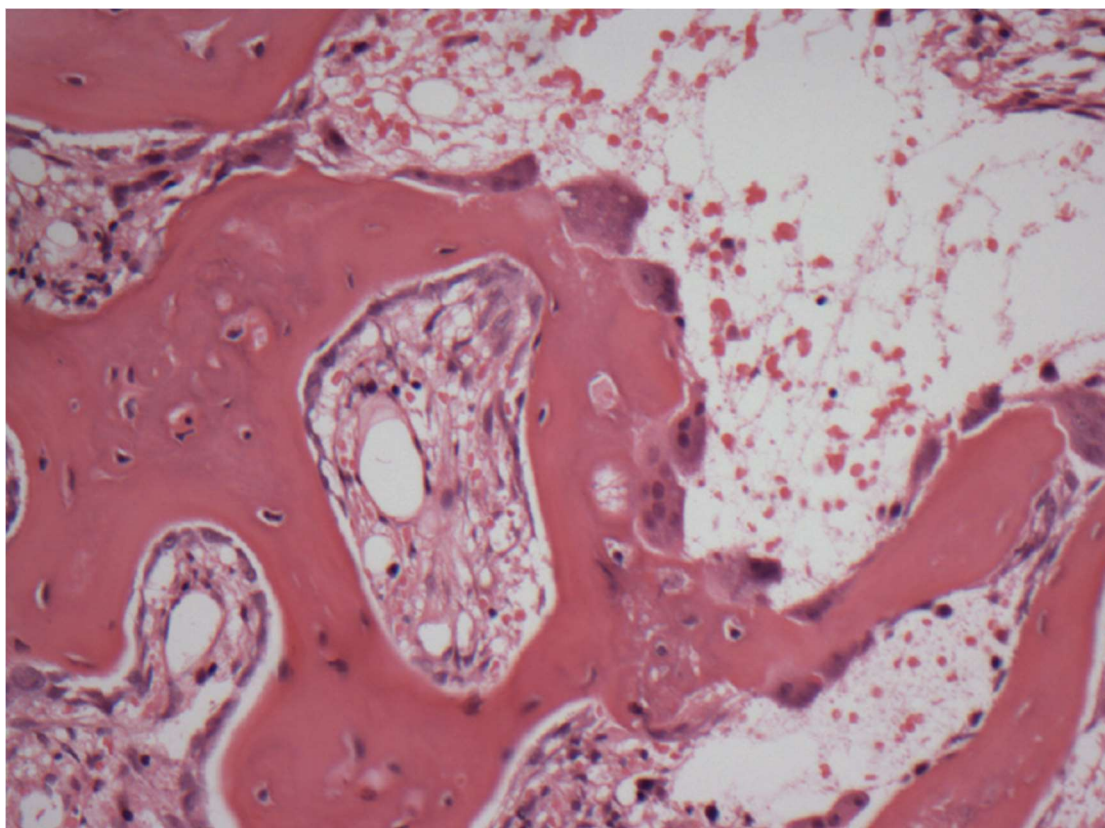
Histology Slide 2: The normal bone architecture is replaced by fibroblastic tissue of low cellularity with minimal cellular atypia. Small islands of woven bone are being produced within the fibroblastic tissue. H/E stain, original magnification x20 (inset x2)











References:

- 1: **Huvos A, Butler A, Bretsky S.** Osteogenic sarcoma associated with Paget's disease of bone. *Cancer* 1983; **52**: 1489–1495.
- 2: **Paget J.** On a Form of Chronic Inflammation of Bones (Osteitis Deformans) *Med Chir Trans.* 1877;60: 37 – 64
- 3: **Barker DJP, Clough PWL, Guyer PB, Gardner MJ.** Paget's disease of bone in 14 British towns. *Br MedJ* 1977;1:1181-3.
- 4: **Reasbeck JC, Goulding A, Campbell DR, Beale LR, Stewart RD.** Radiological prevalence of Paget's disease in Dunedin New Zealand. *Br Med J (Clin Res Ed.)* 1983 18;286
- 5: **Gardner MJ, Guyer PB, Barker DJP.** Radiological prevalence of Paget's disease of bone in British migrants to Australia. *BMJ* 1978 i:1655–1657
- 6: **Greditzer HG, McLeod RA, Unni KK, Baebout JW.** Bone Sarcomas in Paget disease. *Radiology.* 1983;146:327-333
- 7: **Smith J, Botet JF, The SDJ.** bone sarcomas in Paget's disease: a study of 85 patients. *J Rad* 1984;152;583±90

- 8: **Hansen MF, Seton M, Merchant A.** Osteosarcoma in Paget's disease of bone. *J Bone Miner Res.* 2006 Dec;21(Suppl 2):P58–P63
- 9: **Clayer M,** The many faces of osteosarcoma on plain radiographs, *ANZ J Surg* 2014 85;(1-2): 22-26
- 10: **Schajowicz F, Arauto ES, Berenstein M.** Sarcoma complicating Paget's disease of bone. A clinicopathological study of 62 cases. *J Bone Joint Surg* 1983 55B:299-307.
- 11: **Shaylor PJ, Peake D, Grimer R, Carter SR, Tillman RM, Spooner D.** Paget's osteosarcoma : no cure in sight. *Sarcoma* 1999 3;(1):191-192
- 12: **Franchi A, Bacchini P, Rocca C, Bertoni F.** Central low-grade osteosarcoma with pagetoid bone formation: a potential diagnostic pitfall. *Modern Pathology.* 2004;17(3):288-291.
- 13: **Malhas AM, Sumathi VP, James SL, et al.,** Low-Grade Central Osteosarcoma: A Difficult Condition to Diagnose. *Sarcoma*, 2012, Article ID 764796, doi:10.1155/2012/764796
- 14: **Kurt AM, Unni KK, McLeod RA, and Pritchard DJ,** Low-grade intraosseous osteosarcoma, *Cancer*, 1990; 65(6):1418–1428